

## Remarks

Claim 1 is amended to recite that the R<sub>10</sub> group is covalently bonded to the inorganic oxide support via a metal atom. Support for this amendment may be found on pages 10-11, paragraph [0039].

Claim 2 is canceled.

Claims 10-54 are non-elected.

Claims 1 and 3-54 are pending in the subject application.

Claims 1-5 and 7-9 stand rejected under 35 USC §102(b) as anticipated by or, in the alternative, under 35 USC §103(a) as obvious over US Patent No. 4,029,583 to Ho Chang (hereinafter "Ho Chang"), US Patent No. 6,074,555 to Boos (hereinafter "Boos") and US Patent No. 5,667,674 to Hanggi (hereinafter "Hanggi"). This rejection is respectfully traversed.

Claim 1 of the instant application recites a solid comprising inorganic substance and moiety R<sub>10</sub> **covalently bonded to a metal atom on at least one surface of the organic substance**, wherein R<sub>10</sub> is selected from the group consisting of:

-CH<sub>2</sub> OH, -CH(OH)<sub>2</sub>, -CH(OH)CH<sub>3</sub>, -CH<sub>2</sub> CH<sub>2</sub> OH, -C(OH)<sub>2</sub>  
CH<sub>3</sub>,  
-CH<sub>2</sub>CH(OH)<sub>2</sub> and -CH(OH)CH<sub>2</sub>(OH).

These recited R<sub>10</sub> groups possess very low acidity when bonded to the surface of the inorganic oxide. As a result, the inorganic oxide, when utilized in processes for the separation of biological materials, eliminates non-specific binding of the biological material to the inorganic oxide over a wide range of pH values as is demonstrated in the examples of the subject application.

Ho Chang describes a chromatographic inorganic support having a silane-coupling agent bonded thereto (column 4, lines 20-35). A stationary phase P<sub>2</sub> is bonded to the silane-coupling agent and renders the inorganic support hydrophobic in nature. As a result, biological micro molecules may be bound to the support during separation processes (column 10, lines 24-46). The crux of Ho Chang lies in the

hydrophobic support surface, which allows any type of biological material to be bound thereto. However, hydrophobic surfaces do not allow for non-specific bonding of biological materials.

In total contrast, the crux of the instant invention is to eliminate non-specific binding of biological materials to the inorganic support during separation processes. Moreover, Ho Chang does not disclose any of the R<sub>10</sub> groups recited in present claim 1. Ho Chang utilizes large polymers that are bonded to the inorganic support. The differences between the surface chemistry of Ho Chang and the instant claimed invention is illustrated below.

Ho Chang

Claim 1

Support-Si CH<sub>2</sub> CH<sub>2</sub> CH<sub>2</sub> R<sub>1</sub>P<sub>2</sub>

Support-CH<sub>2</sub>OH

As is readily apparent, the claimed invention comprises a hydrophilic group directly bonded onto an inorganic oxide surface and Ho Chang utilizes a hydrophobic group bonded to an inorganic oxide surface. Accordingly, Ho Chang does not disclose every element recited in claim 1. Moreover, there is no motivation provided in Ho Chang or the Office Action for one of ordinary skill in the art to modify the teachings of Ho Chang and arrive at the instantly claimed invention. There is no suggestion or motivation to utilize a hydrophilic group instead of a hydrophobic group. Thus, Ho Chang does not anticipate or render obvious claims 1-5 and 7-9, and withdrawal of the rejection is respectfully requested.

Boos describes a chromatographic support having hydrophobic inner pore surfaces formed of fatty acid esters and hydrophilic outer surfaces (abstract). This allows certain biological substances to bond to the inner pore surfaces while not bonding to the hydrophilic outer surface. The support is formed by reaction with a diol coupling agent, followed by the formation of an ester linkage, and subsequent enzymatic cleavage to remove the ester and form a “diol phase” on the outer surface of the support (columns 3 and 4).

As above-mentioned, the crux of the present invention resides in the elimination of non-specific bonding of biological materials to the chromatographic support over a wide range of pH values. This is accomplished by selecting R<sub>10</sub> moieties or surface groups that have low acidity (i.e., the electron withdrawing character of the atom bonded to the inorganic oxide surface and the acidity of the terminating group) that are directly bonded to the inorganic oxide surface. In contrast, Boos utilizes an ether oxygen atom that is bonded to the support surface that results in a highly acidic hydrophilic group due to the electron withdrawing character of the oxygen atom. The differences between the claimed invention and Boos is illustrated by the following:

Boos

Support-O -CH<sub>2</sub> -CHOH -CH<sub>2</sub> OH

Claim 1

Support-CH<sub>2</sub>OH

The acidity of the Boos hydrophilic group is significantly higher than the claimed R<sub>10</sub> group. Boos is completely silent with regard to the effect that acidity of the hydrophilic surface groups has on separation processes involving biological materials. Moreover, the preferred hydrophilic group set forth in Boos is 2, 3-dihydroxypropyl group (column 4, lines 6 and 7) which possesses an acidity of more than 10,000 times that of the R<sub>10</sub> groups recited in claim 1 (i.e., the pKa of 2,3-dihydroxypropyl is about 12 and the pKa of the groups recited in claim 1 is about 16). This would motivate the artisan to utilize highly acidic hydrophilic groups, which is in contrast to the presently claimed invention.

Accordingly, Boos does not set forth all of the elements in present claim 1, nor is there any suggestion or motivation set forth in Boos, or otherwise, to modify the teaches therein and arrive at the presently claimed invention. Boos does not anticipate or render obvious claims 1-5 and 7-9, and withdrawal of the rejection is respectfully requested.

Hanggi, describes a chromatographic support having a polymerization product of a silane, including two or three olefinic groups, which yields a hydrophobic surface

(abstract). The carbosilane polymer on the surface of the support allows adsorption of biological materials thereon. This adsorption is non-specific in nature.

As above-mentioned, the crux of the claimed invention lies in the low acidity of the hydrophilic surface groups bonded directly to the inorganic support. There is no mention in Hanggi of the claimed R<sub>10</sub> groups. The differences between the carbosilane polymers bonded to the inorganic support set forth in Hanggi and the R<sub>10</sub> groups bonded to the inorganic support recited in instant claim 1 is illustrated as follows:

Hanggi

Support-Si -(CH<sub>2</sub>)<sub>m</sub> CH=CH<sub>2</sub>

Claim 1

Support-CH<sub>2</sub>OH

It is readily apparent from the illustrations that the R<sub>10</sub> groups set forth in present claim 1 are significantly different that the carbosilane groups described in Hanggi. Accordingly, the elements set forth in claim 1 are not disclosed by Hanggi. Moreover, there is no motivation or suggestion in Hanggi, or otherwise, to modify the teachings therein and arrive at the instantly claimed invention. Hanggi suggests using a hydrophobic group bonded to the inorganic oxide surface. Thus, Hanggi does not anticipate or render obvious claims 1-5 and 7-9, and withdrawal of the rejection is respectfully requested.

Claim 6 stands rejected under 35 USC §103(a) over Ho Chang, Boos and Hanggi, further in view of US Patent No. 5,055,194 to Goetz. This rejection is respectfully traversed.

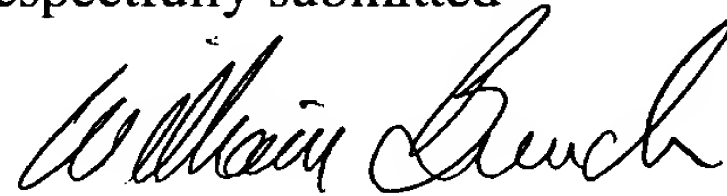
Goetz discloses the use of silica coated magnetically susceptible particles for use in chromatographic separations (abstract). Goetz does not rectify the deficiencies of Ho Chang, Boos or Hanggi. In particular, there is no mention in Goetz of the R<sub>10</sub> groups recited in claim 1 of the present application. Moreover, there is no motivation or suggestion in Goetz to modify the teachings of Ho Chang, Boos, or Hanggi and arrive at the claimed inorganic oxide having lower acidic hydrophilic groups directly bonded thereto. Thus, Goetz does not render obvious claim 6 of the present application, and withdrawal of this rejection is respectfully requested.

Claim 9 stands rejected under 35 USC §103(a) over Boos in view of Ho Chang. This rejection is respectfully traversed.

For the identical reasons as set forth above with respect to the rejection of claims 1-5 and 7-9, neither Boos nor Ho Chang suggest or motivate one of ordinary skill in the art to modify the teachings therein and arrive at the instantly claimed invention (i.e. there is no suggestion to utilize the claim low acidic hydrophilic groups directly bonded to the inorganic oxide support). Since claim 9 is dependent upon claim 5, claim 9 also distinguishes over Boos and Ho Chang, either individually or in combination. Thus, the Applicant respectfully requests withdrawal of the rejection.

In view of the above remarks, Applicant respectfully submits that the above-mentioned patent application is now in condition for allowance. Applicant respectfully requests notification to that effect in the form of a Notice of Allowability.

Respectfully submitted



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